PISCES

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Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional research previously applied in human subjects

Summary

ID

NL-OMON57511

Source
Onderzoeksportaal

Brief title
Placebo effect In Spinal Cord Electrical Stimulation for Pain (PISCES)

Condition

- Other condition

Synonym
Persistent spinal pain syndrome type 2

Research involving
Human

Sponsors and support

Primary sponsor: Sahlgrenska University Hospital
Source(s) of monetary or material Support: Rijnstate

Intervention

- Medical device

Explanation

N.a.

Outcome measures

Primary outcome

The primary outcome measure is the difference in change in neuropathic leg pain intensity scores between a 3-month period with subthreshold stimulation and a 3-month period with sham stimulation, as compared to baseline. Pain intensity is measured using to the Numeric Rating Scale (NRS; 0 no pain, 10 worst imaginable pain).

Secondary outcome

Difference in neuropathic leg pain intensity score at 12 months follow up, after the patient has received their preferred stimulation form, as compared to baseline. Pain intensity is measured using to the Numeric Rating Scale (NRS).
Quality of life at 3, 6 and 12 months follow-up compared to baseline, measured using the EuroQoL-5D-5L (EQ-5D-5L) questionnaire.
Physical functioning at 3, 6 and 12 months follow-up compared to baseline, measured using the Oswestery disability index (ODI) questionnaire.
Sleep quality at 3, 6 and 12 months follow-up compared to baseline, measured using the Pittsburgh Sleep Quality Index (PSQI) questionnaire.
Medication use at 3, 6 and 12 months follow-up compared to baseline, queried during the follow-up visit.
Number of hours worked per week at 3, 6 and 12 months follow-up compared to baseline, queried during the follow-up visit.

Study description

Background summary

Up to 20% of patients who have undergone lumbar spinal surgery experience new or persistent back/leg pain, leading to reduced functionality and quality of life. This condition is known as persistent spinal pain syndrome type 2 (PSPS2). SCS is an established and safe minimally invasive treatment for PSPS2 when no further surgery is indicated and conservative therapies have been found to be ineffective.

However, current evidence for the effectiveness of SCS therapy is based on studies comparing different forms of stimulation and studies comparing SCS with conventional medical management. Sham-controlled studies, comparing active and sham stimulation, were lacking until recently as traditional stimulation methods relied on the patient feeling the stimulation (i.e., paresthesia).

Technological advances have led to the development of paresthesia-free (subthreshold) stimulation forms, which allows for the execution of sham-controlled studies. A recent study showing no significant difference in long-term effectiveness between SCS and sham stimulation suffers from significant methodological shortcomings. This necessitates further sham-controlled studies to determine if SCS is an adequate treatment for PSPS2.

Study objective

The aim of the PISCES study is to evaluate the long-term effectiveness of SCS by comparing a paresthesia-free form of stimulation that the patient does not feel, with sham stimulation in which no stimulation is given. The study will focus on patients with treatment-resistant leg pain after lumbar spine surgery (persistent spinal pain syndrome type 2, PSPS2), which is the most common patient group treated with spinal cord stimulation. The data documented within the PISCES study may support the evidence for spinal cord stimulation as an effective and cost-efficient long-term treatment for PSPS2.

Study design

According to standard clinical practice, research participants are implanted with electrode(s) during an initial surgery, which are inserted into the epidural space posterior to the spinal cord dorsal columns, with the aim of obtaining the best possible coverage of the painful area. Subsequently, patients undergo a trial phase of 2 weeks with an external Boston Alpha Prime battery providing subthreshold stimulation that the patient does not feel. In patients with adequate pain relief (>50% pain reduction) after the trial period, a permanent battery is placed under the skin and will be connected to the electrode(s). Patients will then be randomized into either the subthreshold stimulation or sham (inactive) stimulation group. Subsequently, subjects will undergo a four-week period where patients can recover from their surgery (wound pain) and where stimulation settings will be optimized. After the optimization period, patients will enter either group 1 (active stimulation) or group 2 (sham stimulation). After 3 months, patients will switch to the other group according to a crossover design where they will receive the other stimulation form until the 6-month follow-up. Then, patients can choose to switch to the group with the stimulation they found most effective, while remaining in that respective group until the end of the study. Patients will be aware that they will receive two different stimulation forms and will be informed that one of the stimulation forms is in fact placebo stimulation. Both the physician who implanted the system and the patient will be unaware of the stimulation form received (a double-blind design) during the entire study period. Activation/deactivation and reprogramming of the stimulation will be performed by a research nurse, who is the only one aware of which group the patient belongs to.

Intervention

There are two intervention groups: treatment with subthreshold stimulation or sham (inactive) stimulation.

Study burden and risks

Specifically for this study, patients are asked to complete a number of questionnaires before surgery (baseline) and at 3, 6, and 12 months after the optimization period. These are questionnaires that are also (partly) used as standard at the Rijnstate Hospital, taking approximately 20 minutes to complete. Study participants will receive placebo (inactive) stimulation for a period of 3 months. Treatment with placebo stimulation may be associated with suboptimal pain relief. This risk is to a large extend offset by the possibility for patients to decide at any time, but after testing the stimulation form for at least 1 week due to the carryover effect, to prematurely switch to the other stimulation group to receive the other stimulation form. The patient can also at any time decide to switch back to the previous stimulation group after testing the stimulation form at least 1 additional week.

We do not anticipate any additional risks, complications, and/or side effects beyond the regular risks and side effects associated with the implantation of a spinal cord stimulation system.
These risks include:

Possible allergic skin rash or a local hematoma at the injection site are side effects of spinal cord neurostimulation. There is a very small chance of epidural bleeding (not higher than with any form of regional anesthesia) and risk of system infection. In general, infection occurs in 2% of implanted patients at Rijnstate Hospital. These are usually superficial skin infections, but attention should be paid to deeper infections. Therefore, patients routinely receive preoperative prophylactic antibiotics and are informed about infection symptoms (pain, redness, fever, stiff neck). At the start of treatment, patients are contacted twice a week by the pain center regarding possible infection or meningitis symptoms.

Contacts

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Trial sites

Trial sites in the Netherlands

Rijnstate
Target size: 10

Listed location countries

Sweden, United Kingdom, Norway, Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- History consistent with PSPS2 of at least 6 months. The patient experienced no effect of conservative treatments and has been assessed as not eligible for further spinal surgery.
- Patients between 18-70 years of age.
- Average perceived pain intensity in the legs of 5 or higher and average perceived pain intensity in the back lower than 3, measured with the validated 11-box NRS (0 no pain, 10 worst imaginable pain).
- The patient should have been informed verbally and in writing about the study and should have provided informed written consent to participate.
- Adequate pain relief effect (>50%) after a two week trial with test stimulation.

Exclusion criteria

- Subject is unable to understand or operate the SCS device.
- Subject currently has an active implantable device including pacemakers, spinal cord stimulator or intrathecal drug delivery system.
- Ongoing coagulation disorder.
- Ongoing abuse of alcohol, drugs, or prescription opioids.
- Active debilitating psychiatric illness.
- Active malignancy.
- Condition with increased general infection sensitivity, such as known immunodeficiency.
- Expected lifespan <1 year.
- Ongoing local infection or other skin disease where the IPG is planned to be placed.

- Pregnancy.
- Participation in another study.

Study design

Design

Study phase:	N/A
Study type:	Interventional research previously applied in human subjects
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2025
Enrollment:	10
Duration:	14 months (per patient)
Type:	Anticipated

WORLD

Recruitment status:	Pending
Start date (anticipated):	01-09-2024
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Product type:	Medical device
Generic name:	Spinal cord stimulation
Registration:	Yes - CE intended use

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N.a.

Ethics review

Approved WMO Date:	23-04-2025
Application type:	First submission
Review commission:	METC Oost-Nederland

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT06585033
Research portal	NL-009659